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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,092	03/21/2002	Jun Ishizaki	220738 USOPCT	7124

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EXAMINER	
SAIDHA, TEKCHAND	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 07/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,092	ISHIZAKI ET AL.	
	Examiner	Art Unit	
	Tekchand Saidha	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *4-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 March 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The Preliminary Amendment dated March 21, 2002 is acknowledged. According to this preliminary amendment claim 3-18 were amended. Claims 1-18 are present in this application.

2. ***Election***

Applicant's election with traverse of Group I, filed June 18, 2004, original claims 1-3, drawn to a polypeptide of SEQ ID NO: 30 (residues 1-123) is acknowledged. The traversal is on the ground(s) that there is a **unity of invention** with respect to Groups I, II III and IV. Applicant traverses the lack of unity requirement (beginning at page 2) by stating that the unity of invention standard must be applied in national stage applications. Applicants though do not cite sections of MPEP § 1800 in support of their statements, but instead cite Annex B, page AI-63 and more specifically example 17. In response to applicant's statements, it is noted that the unity of invention standard *was* applied to original claims 1-18 in evaluating the claims for unity of invention and restricting the claims according to 35 U.S.C. 121 and 372. MPEP § 1893.03(d) states, "If the examiner finds that a national stage application lacks unity of invention under § 1.475, the examiner may in an Office action require the applicant in the response to that action to elect the invention to which the claims shall be restricted".

Also, according to PCT Rule 13.2, unity of invention exists only when the shared same or corresponding technical feature is a contribution over the prior art. The inventions of original claims 1-18 do not relate to a single general inventive concept because the shared technical features of the claimed polypeptide and polynucleotide lack novelty or inventive step and therefore, do not make these technical features a contribution over the prior art. In accordance with MPEP § 1893.03(d), the examiner properly applied the unity of invention standard to original claims 1-18 in the instant application.

Applicants' claim 4 is drawn to a DNA that encodes an amino acid sequence of SEQ ID NO: 30, wherein one or more amino acid are substituted, deleted, inserted or added. Such a sequence has no sequence homology limitation and will read on any DNA sequence encoding a protein having Phospholipase A2 activity. Relevant prior art references are **Accession No. U95301**, a Phospholipase A2, (1997); or DNA encoding a secreted Phospholipase A2 taught by **Cupillard et al. [J. Biol. Chem. 272 (25): 15745-15752, June 20 1997]**.

Beginning at the top of page 2, applicant cites Example 17, Part 2 of Annex B to the Administrative Instructions Under the PCT, which states:

Example 17
Claim 1: Protein X.
Claim 2: DNA sequence encoding protein X.
Expression of the DNA sequence in a host results in the production of a protein which is determined by the DNA sequence. The protein and the DNA sequence exhibit corresponding special technical features. Unity between claims 1 and 2 is accepted.

Applicant argues the examiner should withdraw the lack of unity requirement with respect to claims of Group I, drawn to the special technical feature of a polypeptide, and co-examine the claims of Group II with the elected claims of Group I. Applicants further argue as per PCT Rule 13.2 that Groups I and II share the same corresponding special technical feature in the protein of Group I and the DNA which encodes the protein of Group I is the DNA of Group II and, as such, should be rejoined and examined in the present application. Further, the special technical feature of Group I and Group III can clearly be seen to be the protein of Group I and, as such, it is submitted that Group III should also be rejoined with Groups I and II and examined in the present application. Further, it can be seen that the special technical feature of Group IV is the protein of Group I and, therefore, the claims of Group IV should also be rejoined with the claims of Group I, II and III and examined in the present application.

Applicant's argument is not found persuasive. According to PCT Rule 13.2, unity of invention exists only when there is a shared same or corresponding special technical feature among the claimed inventions. The DNA of claim 4, which is drawn to any DNA [subjected to the modification of one or more additions, deletions, substitution or insertions] as per the claim recitation is interpreted to read on any DNA sequence of any similarity to SEQ ID NO: 29 and capable of encoding a Phospholipase A2, is encompassed by such a DNA and that, when expressed in a host, results in the production of proteins that *do not* correspond to the protein of Group I. Therefore, the DNA of Group II, particularly the DNA of claim 4, does not share a corresponding special technical feature with the polypeptide of Group I, and thus the inventions do not have unity of invention. Furthermore, according to PCT Rule 13.2, unity of invention exists only when the shared same or corresponding technical feature is a contribution over the prior art. The inventions of Groups I and II do not have unity of invention because the technical feature of Group II do not contribute over the prior art.

Thus, there is no unity of invention between the enzyme of Group I and the antibody and Phospholipase inhibitor screening method of III and IV, because the antibody and the method are

not needed to make and use the enzyme or that the enzyme can be used in a distinct method such an in a treating composition. As per the rejoinder of method claims when the product claims become allowable, Applicants are referred to the previous Office Action for the rejoinder notice. Thus, the determination of lack of unity is proper under the PCT treaty.

The lack of unity determination is not made FINAL yet, because of the newly introduced prior art cited in this Office Action.

3. **Claims withdrawn**:

Claims 4-18 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed.

4. Claims 1-3 are pending and under consideration in this examination.

5. ***Priority***

Acknowledgment is made of applicants' claim for priority based on an application filed in Japan on September 18, 1999.

4. ***Specification***

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

5. ***35 U.S.C. § 112, first paragraph***

Claim 3 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a human secretory phospholipase A2 of SEQ ID NO: 30, does not reasonably provide enablement for any phospholipase wherein SEQ ID NO: 30 has been modified to any extent i.e., wherein one or more amino acid residues are added, inserted or deleted or substituted and having Phospholipase A2 activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of phospholipases-A2 broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this

case the disclosure is limited to the nucleotide and encoded amino acid sequence of phospholipase-A2 of SEQ ID NO : 30.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications of phospholipase-A2 of SEQ ID NO: 30 by addition, deletion, substitution or insertion, because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting phospholipase-A2 activity; (B) the general tolerance of phospholipase-A2 to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any phospholipase-A2 residues with an expectation of obtaining the desired biological function; and (D) the specification provides

insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claim broadly including obtaining Phospholipase(s)-A2 by enormous number of amino acid modifications of SEQ ID NO: 30. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of Phospholipase(s)-A2 having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is improper and undue in making the modified enzyme. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

6. ***Claim Rejections - 35 USC § 112*** (second paragraph)

Claims 1-3 are rejected under 35 U.S.C.§ 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, line 1, recites 'from first Asn' to 123rd Cys of...SEQ ID NO: 30'. Similarly claim 2, line 1, recites 'from 19th Asn' to 123rd Cys of...SEQ ID NO: 30'. However, according to

Applicants' computer readable form of the sequence listing the correspondence of the amino acid position as claimed is not correct, and therefore, the claims are indefinite. SEQ ID NO: 30 carries a pre-sequence or signal sequence of about 19 amino acids which need to be accounted in the numbering of the claims.

Correcting the claim language to recite 'SEQ ID NO: 30' or other suitable modifications will over come this rejection.

Claim 3 is included in the rejection for failing to correct the defect present in the base claim(s).

7. ***35 U.S.C. § 101***

35 U.S.C. §101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 1-3 are rejected under 35 U.S.C. § 101 because the claimed invention is directed toward non-statutory subject matter.

In the absence of the hand of man, naturally occurring proteins and/or nucleic acids are considered non-statutory subject matter. *Diamond v. Chakrabarty*, 206 USPQ 193 (1980).

This rejection may be overcome by amending the claims 1-3 to recite wording such as "An isolated protein".

8. ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 3 is rejected under 35 U.S.C. 102(b) as being anticipated by any one of the following references: (1). Accession No. S17860, (2). US Patent 5656602 (issued 1997), (3) Accession No. AAR10126, (4) Accession No. AAR63055, (5) Accession No. U95301, and (6) Cupillard et al. [J. Biol. Chem. 272 (25): 15745-15752, June 20 1997].

Claim 3 is drawn to an amino acid sequence of SEQ ID NO: 30, wherein one or more amino acid are substituted, deleted, inserted or added. Such a sequence has no sequence homology limitation and will read on any protein sequence having Phospholipase A2 activity. Prior art references 1-4 disclose

proteins having Phospholipase A2 activities and amino acid sequence similarity between 45% and 51% compared to SEQ ID NO: 30. The references anticipates the claim.

Prior art reference 5-6 disclose proteins having Phospholipase A2 activities. The claims are written so broadly, and therefore anticipated by the references.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha (Ph.D.) whose telephone number is (571) 272-0940. The examiner can normally be reached on Monday-Friday from 8:15 am to 4:45 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group in the Technology Center is 703 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is 571 272-1600.

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July 18, 2004